Human papillomavirus vaccination for boys

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Abstract

Question In Canada, generally provincial human papillomavirus (HPV) vaccination programs exist for only the female population. What should I recommend when parents and teenage boys ask about male HPV vaccination?

Answer The quadrivalent HPV vaccine is effective and will reduce the incidence of disease in boys and girls. The quadrivalent HPV vaccination is approved and recommended for both boys and girls in Canada. Public funding for male vaccination is available in Prince Edward Island and Alberta. The remaining provinces and territories will need to consider cost-effectiveness analyses before expanding their female-only vaccination programs to include the male population.

Vaccin contre le virus du papillome humain pour les garçons

Résumé

Question Au Canada, les programmes provinciaux de vaccination contre le virus du papillome humain (VPH) sont généralement réservés à la population féminine. Que devrais-je recommander aux parents et aux adolescents qui me posent des questions à propos de la vaccination de la population masculine contre le VPH?

Réponse Le vaccin quadrivalent contre le VPH est efficace et réduira l'incidence de la maladie chez les garçons et les filles. Le vaccin quadrivalent contre le VPH est homologué et recommandé à la fois pour les garçons et pour les filles au Canada. Des fonds publics sont accessibles pour la vaccination chez les garçons à l'Île-du-Prince-Édouard et en Alberta. Les autres provinces et territoires devront envisager de faire des analyses de rentabilité avant d'élargir leurs programmes de vaccination réservés aux filles pour inclure la population masculine.

Human papillomavirus (HPV) is a double-stranded DNA virus. It is the most common sexually transmitted infection[1-4] and is transmitted sexually by both sexes[2] and vertically from an infected maternal genital tract.[3,5] Infection has been documented in the absence of penetrative sexual intercourse.[5] Although initially thought to affect primarily women, the incidence of genital HPV infection among men is similar to that among women.[6] Transmission is common, as median time to clearance of infection is 6 months or more.[2] The peak rise for HPV infection is within 10 years of the first sexual experience.[7] More than 100 distinct genotypes of HPV have been described,[8] of which at least 40 types are able to infect the genital tract.[3,5,9]

In a study of 5000 females aged 13 to 86 years, Moore et al found that HPV had a prevalence of 17% in Canada[7]; however, little is known about the prevalence or incidence of HPV in men. In a population study of 262 heterosexual men in Vancouver, BC,[7,10] Ogilvie and colleagues reported that infection with any HPV type had a prevalence of 70% and that preventable genotypes (6, 11, 16, and 18) had a prevalence rate of 35%.[10]

In the long term, HPV causes both benign and malignant anogenital disease, as well as head and neck lesions.[7] According to the American Academy of Pediatrics, each year in the United States, 15 000 women and 7000 men are diagnosed with cancers caused by HPV types 16 and 18.[4] Infection with the high-risk oncogenic HPV types 16 and 18 is a known cause of cervical cancer,[1,11] and is associated with cancers of the penis, anus, mouth, oropharynx,[1,3,7] larynx, vulva, and vagina.[1,3] In fact, almost all cases of cervical cancer can be traced to infection with oncogenic HPV types 16 and 18.[4,8] In men, 92% of anal cancer cases, 63% of penile cancer cases, and 89% of oral or oropharyngeal cancer cases are attributed to HPV types 16 and 18.[8]

More than 90% of genital warts are caused by the nononcogenic HPV types 6 and 11,[4,7] and 20% to 50% of cases involve co-infection with oncogenic types.[7] Two Canadian studies in Manitoba and British Columbia[9,12] estimated anogenital warts to cause a considerable burden of disease, with incidence of 131 to 154 per 100 000 population in men and 120 per 100 000 in women.[7] Prevalence of anogenital warts

was 157 to 165 per 100 000 population in men and 128 to 140 in women.[7]

Vaccination

The quadrivalent HPV vaccine (HPV4) is directed against HPV types 6, 11, 16, and 18, and has been licensed by the Food and Drug Administration for use in the female population since 2006[13] and in the male population since 2009.[14] Indications for the 9- to 26-year-old male age group were initially for prevention of genital warts caused by HPV types 6 and 11.[14] Prevention of anal cancer in the male and female populations was added as an indication in 2010.[13] In 2011, the Advisory Committee on Immunization Practices recommended routine use of the HPV4 vaccine in boys 11 to 12 years old, as well as catch-up vaccination in adolescent boys and men aged 13 to 21 years.[13]

The American Academy of Pediatrics 2012 policy statement recommends immunization against HPV for all 11- to 12-year-old children.[4] The most recent Canadian Paediatric Society position statement from 2008 recommended routine vaccination of girls.[3] **Table 1**[7,15-18] presents a summary of HPV immunization programs by province.

Efficacy

In clinical trials, HPV4 is safe and highly effective (90% to 100%) against persistent infection with HPV types 6 and 11 and genital warts in women and men.[19] Efficacy of HPV4 in 10- to 15-year-old males was initially based on a (prelicensure) noninferiority immunobridging study by Block et al.[20] The study included 506 girls and 510 boys aged 10 to 15 years old and 513 young women aged 16 to 23 years.[20] Anti-HPV titres in girls and boys were 1.7-fold to 2.7-fold higher compared with the young women.[20] Giuliano and colleagues enrolled 4065 adolescent boys and men aged 16 to 26 years from 18 countries in a randomized, placebo-controlled, double-blind trial and reported that HPV4 reduced the incidence of external genital lesions related to HPV types 6, 11, 16, and 18 by 90% compared with placebo, and reported the efficacy in the intention-to-treat population as 65% (95% CI 45% to 78%).[6] In a subsequent study, Goldstone et al randomized 4065 males to assess the efficacy of HPV4 against disease related to nonvaccine HPV types and found that HPV4 protected males against most vaccine HPV-type (6, 11, 16, 18) related anogenital disease.[21]

Safety

More than 40 million doses[13] of HPV4 were administered in the first 5 years of routine administration in American girls, with few cases of anaphylaxis and no other reported vaccine-specific adverse effects.[9] An anaphylaxis rate of 2.6 per 100 000 doses of HPV4 vaccine was reported from Australia, which was higher compared with rates reported for other vaccines.[22] The most common adverse events are injection site pain, swelling, and erythema.[7,13]

Target population

Australia was the first country to vaccinate girls against HPV and has been doing so since 2007. Donovan et al identified trends in diagnosis of genital warts in Australia before and after initiation of female HPV4 vaccination.[19] Incidence of genital warts declined from 12% to 5% in women and from 12% to 9% in heterosexual men according to national surveillance network data.[19] The decline seen in men was possibly due to reduced partner exposure to vaccine-specific HPV infection because young women had been vaccinated.[19]

In 2013, Australia became the first nation to vaccinate the male population against HPV.[23] Mathematical model prediction of what outcomes would be after 6 years of male vaccination suggested relative reduction in the incidence of genital warts would be 70% in the female population and 65% in the male population, and by 2030 about 90% in female and male populations.[23]

Economic considerations

Many economic studies regarding HPV vaccination exist in the literature, ranging from assessment of economic burden of disease to examination of public health effects of gender-neutral vaccination. Hu and Goldie estimated the direct medical costs of 7 noncervical HPV-related conditions and the economic burden of noncervical HPV disease to be $418 million (US) (range $160 million to $1.6 billion) for new cases in 2003, with greater than 60% of the total burden related to HPV types 6 and 11.[1]

Elbasha and Dasbach assessed the public health effects and value of vaccinating boys with HPV4 in the United States using mathematical models and found that the incidence and prevalence rates of all HPV-related (types 6, 11, 16, and 18) disease among the female and male populations would have additional decreases with the addition of male vaccination.[24] While in a recent study in Norway vaccinating boys was seen as beneficial, increasing coverage in girls was uniformly more effective, economical, and could prevent nearly as many HPV-related cancers among men through herd immunity.[25] When considering inclusion of the male population in HPV immunization programs in Canada, a program including boys is predicted to be cost-effective only when immunization coverage is lower than 50% among girls.[8]

Special populations

It is generally thought that men who have sex with men and immunocompromised men are at highest risk of genital warts and HPV-associated cancers, and might have greater benefit from HPV vaccination[11] if it is administered before sexual activity first begins. Men

Table 1. Summary of provincial HPV vaccination programs for the female population

PROVINCE OR TERRITORY	ROUTINE SCHEDULE (DOSES AT 0, 2, AND 6 MO)	DATE OF IMPLEMENTATION OF ROUTINE PROGRAM	CATCH-UP PROGRAMS (DATE OF IMPLEMENTATION)
British Columbia	Grade 6	September 2008	Grade 9 (2008-2011)
Alberta*	Grade 5	September 2008	Grade 9 (2009-2012)
Saskatchewan	Grade 6	September 2008	Grade 7 (2008-2009)
Manitoba	Grade 6	September 2008	Grade 6; those born on or after January 1, 1997; and those born between 1986 and 2005 with increased risk of HPV infection who started the vaccine series before March 31, 2014[15,16]
Ontario	Grade 8	September 2007	Grades 9-12[17]
Quebec	Grade 4 (doses 1 and 2); in third y of secondary school (dose 3)	September 2008	Age 9-13 y (high risk of HPV infections) Age 14-17 y Age 9-17 y (in First Nations communities) Third y of secondary school (2008-2013)
New Brunswick	Grade 7	September 2008	Grade 8 (2008-2009)
Nova Scotia	Grade 7	September 2007	Grade 10 (2009-2010 only) Grade 8 (2010-2011 only)
Prince Edward Island*	Grade 6	September 2007	Grade 9 (2009-2010 only)
Newfoundland and Labrador	Grade 6	September 2007	Grade 9 (2008-2010)
Northwest Territories	Grade 4	September 2009	Grades 11 and 12 (2009-2010) Grades 10 and 11 (2010-2011) Grades 9 and 10 (2011-2012) Grade 9 (2012-2014)
Yukon	Grade 6	September 2009	Grades 7 and 8
Nunavut	Grade 6	March 2010	Girls who are not in grade 6 but remain eligible since April 2010[18]

HPV—human papillomavirus.
*Male vaccination included in this province.
Adapted from National Advisory Committee on Immunization.[7]

who have sex with men might not benefit if they do not have access to the subsidized vaccine and are exposed to unvaccinated men.[19]

Conclusion

The quadrivalent HPV vaccine is effective and will reduce the incidence of disease in the male and female population. Currently in Canada, HPV4 vaccination is approved and recommended for both sexes. However, male vaccination is not publicly funded except in Prince Edward Island and Alberta. Remaining provinces and territories will need to consider cost-effective methods before expanding their female-only programs to include male or special populations, while improving female uptake in current programs.

Competing interests
None declared

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